

Original Article

Adrenal cortical adenoma with the maximal diameter greater than 5 cm: can they be differentiated from adrenal cortical carcinoma by CT?

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Abstract: To study the computed tomographic findings of adrenal adenoma with the maximal diameter greater than 5 cm and to discuss whether such tumor can be differentiated from adrenal carcinoma by CT examination. Fourteen consecutive patients with adrenal adenoma with the maximal diameter larger than 5 cm, proven pathologically, were enrolled. All patients underwent non-enhanced and contrast-enhanced CT examination. The CT findings, including size, shape, edge, density on non-enhanced CT and schedule of reinforcement after contrast administration for each lesion were retrospectively analyzed. CT data of 13 patients with adrenocortical carcinoma were also evaluated to determine whether differentiating characteristics existed. The maximal diameter of the 14 masses of adenoma ranged from 5.5 cm to 20 cm (mean, 10 cm). One mass showed lobulated, the rest 13 masses showed rounded or ovoid. Eleven and 3 masses appeared well-circumscribed and ill-circumscribed, respectively. All of 14 masses presented heterogeneous density on non-enhanced CT images with patchy low-attenuation foci or stippled calcification. All of 14 masses revealed moderately to markedly heterogeneous enhancement after contrast administration. None of 14 masses developed local invasion and distant metastasis. Except for recurrence, metastasis and venous tumor emboli which only occurred in the cases of adrenal carcinoma, no definite computed tomographic features could be found that enabled the identification of adenomas with the maximal diameter greater than 5 cm with adrenal carcinomas. The characteristic CT findings of adrenal adenoma with the maximal diameter greater than 5 cm include bulky, well-circumscribed, rounded or ovoid masses, heterogeneous attenuation with low-attenuation foci on non-enhanced CT images and heterogeneous enhancement after contrast administration. The differential diagnosis between such tumor and adrenal cortical carcinoma by CT examination is relatively difficult, such findings as recurrence, metastasis and venous tumor emboli may be of some significance.

Keywords: Adrenal cortical neoplasm, adenoma, carcinoma, diameter, computed tomography, differentiation

Introduction

Most adrenal adenomas have some characteristic radiologic findings: the maximal diameter of tumors are almost always less than 5 cm, relatively homogeneous, and display rapid and relatively uniform enhancement with rapid washout of iodinated or gadolinium-based contrast material. In addition, they often reveal computed tomography (CT) and magnetic resonance (MR) imaging findings associated with intracellular lipid and almost never liquefy; calcification is very rare.

With reference to literatures [1-7], we define those adrenal adenomas whose maximal diam-

eters are more than 5 cm as large adenomas, whereas those adenomas with the maximal diameter less than or equal to 5 cm are defined as small adenomas. Compared with small adenomas, large adenomas are relatively rare.

On account of gigantic tumor and heterogeneous attenuation on CT images, large adrenal adenomas are usually diagnosed as malignant entities by many radiologists, such as adrenal cortical carcinomas, which will influence clinicians' therapeutic decision-making and prognostic prediction. Hence, the purpose of this study was to analyze the computed tomographic findings of 14 patients with large adrenal cortical adenoma, meanwhile, the CT data of 13

Diagnosis and differential diagnosis of large adrenal cortical adenoma by CT

Table 1. Clinical features and pathological subtypes of 14 patients with adrenal cortical adenoma with maximal diameter greater than 5 cm

Case	Sex	Age	Clinical Manifestation	Pathologic Variant
1	Female	45	Hypertension, Headache, Obesity	Cortisol producing adenoma
2	Male	10	Hypertension, Headache, Obesity	Cortisol producing adenoma
3	Male	68	Hypertension, Headache	Cortisol producing adenoma
4	Female	52	Absence of symptoms	Non-functional adenoma
5	Female	49	Hypertension, Headache, Purple striae	Cortisol producing adenoma
6	Male	54	Absence of symptoms	Non-functional adenoma
7	Female	48	Absence of symptoms	Non-functional adenoma
8	Female	70	Hypertension, Headache, Purple striae	Cortisol producing adenoma
9	Male	42	Hypertension, Headache	Cortisol producing adenoma
10	Male	50	Hypertension, Headache, Obesity	Cortisol producing adenoma
11	Female	35	Menstrual disorder, Blushing	Cortisol producing adenoma
12	Male	44	Absence of symptoms	Non-functional adenoma
13	Male	63	Absence of symptoms	Non-functional adenoma
14	Female	37	Absence of symptoms	Non-functional adenoma

Table 2. Clinical features and pathological subtypes of 13 patients with adrenal cortical carcinoma

Case	Sex	Age	Clinical Manifestation	Clinical Outcome
1	Male	52	Hypertension, Adynamia, Nocturia	Uneventful after surgery
2	Male	30	Hypertension, Adynamia, Nocturia	Uneventful after surgery
3	Male	16	Feminization	Uneventful after surgery
4	Male	72	Abdominal pain; Abdominal distention	Uneventful after surgery
5	Female	77	Abdominal pain; Abdominal distention	Uneventful after surgery
6	Female	57	Hypertension, Obesity, Purple striae	Local recurrence
7	Male	52	Hypertension, Obesity	Local recurrence and celiac lymph node metastasis
8	Male	77	Hypertension, Headache,	With tumor thrombus into inferior vena cava
9	Female	45	Virilization	Local recurrence and pulmonary metastasis
10	Male	49	Hypertension, Headache,	Uneventful after surgery
11	Male	60	Hypertension, Adynamia, Nocturia	Uneventful after surgery
12	Female	3	Virilization	Uneventful after surgery
13	Female	40	Menstrual disorder, Blushing	Uneventful after surgery

patients with adrenal carcinoma were also evaluated so as to determine whether large adenoma can be differentiated from adrenocortical carcinoma by CT examination.

Materials and methods

Patients

This retrospective study was approved by our institutional review board, and informed consent was waived. Between January 2009 and July 2013, 18 consecutive patients who were diagnosed as adrenal cortical adenoma with the maximal diameter greater than 5 cm by CT examination were recruited. Four patients were

excluded because the pathologic diagnosis for these tumors were absent. Finally, 14 patients (7 men and 7 women; mean age 48 years, range 10-70 years) with definite pathological diagnosis were included in our study. Meanwhile, 13 patients (8 men and 5 women; mean age 52 years, range 3-77 years) with adrenal cortical carcinoma, pathologically proven, were enrolled in our study.

Imaging protocol

All the 27 patients underwent non-enhanced and enhanced CT examination simultaneously. CT imaging was performed using a Brilliance TM16 (Philips Medical Systems, Best, The



Figure 1. A 35-year-old female with cortisol producing adenoma of the right adrenal gland. A. The mass shows bulky, lobulated appearance and heterogeneous attenuation on non-enhanced CT. B. The mass presents moderately heterogeneous enhancement after contrast administration.



Figure 2. A 52-year-old female with non-functional adenoma of the right adrenal gland. A. The mass shows well-circumscribed, rounded shape and heterogeneous attenuation on non-enhanced CT. B. The mass presents moderately heterogeneous enhancement after contrast administration.

Netherlands) helical scanner with the following parameters: 5 mm slice thickness reconstructions, 120 kV voltage, 200 mA current, and 256×256 matrix. After non-enhanced CT imaging, an intravenous bolus dose of 100 ml of a nonionic iodinated contrast agent (iopromide; Ultravist; Schering) was administered at a rate of 2.5 mL/s for the patients. Enhanced CT images were obtained at 60 s after the contrast agent injection.

Image assessment

Two radiologists who were experienced in performing CT of the adrenal glands and unaware of the clinical, surgical, pathologic results eval-

uated the CT images separately, any disagreements were resolved by consensus. The observations included size, shape, edge, density on non-enhanced CT and schedule of reinforcement after contrast administration, and invasion of adjacent structure and distant metastasis of each mass. For each mass, the maximal cross section was selected and an ovoid or rounded ROI was placed in the center of the section to include as much of the cross-sectional area as possible but avoiding the outermost edge (to prevent partial volume artifact). The same measurements were performed on enhanced CT images, and the ROIs were placed in the corresponding slices. The degree of enhancement after contrast administration of

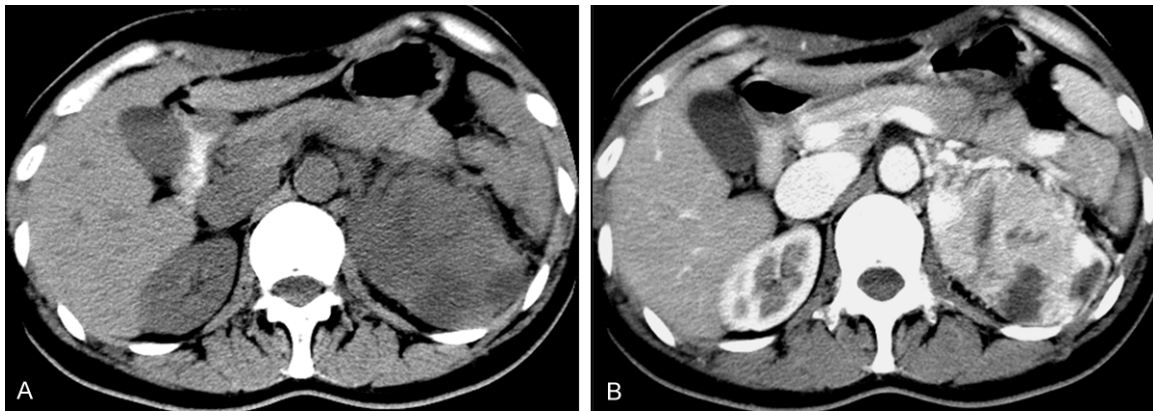


Figure 3. A 68-year-old male with cortisol producing adenoma of the left adrenal gland. A. The mass shows ill-circumscribed, ovoid shape and heterogeneous attenuation on non-enhanced CT. B. The mass presents markedly heterogeneous enhancement after contrast administration.

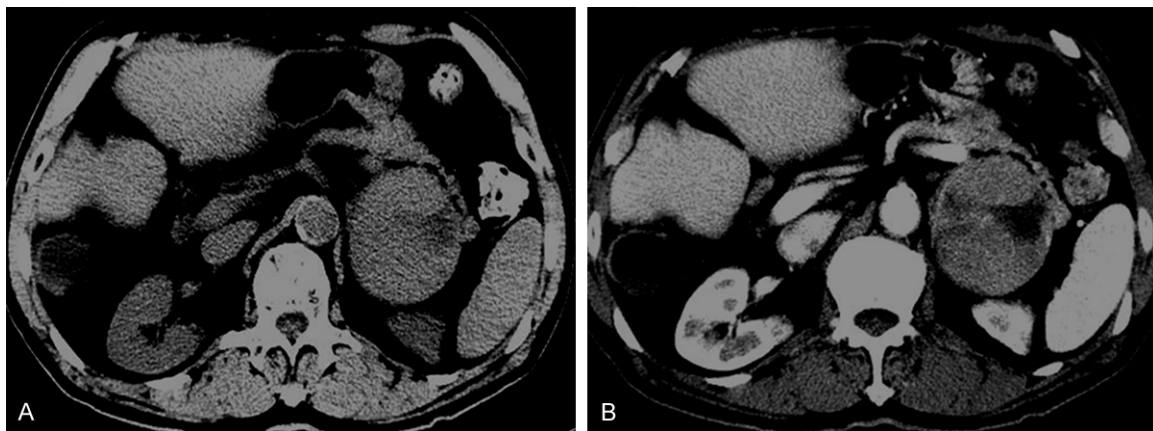


Figure 4. A 49-year-old female with cortisol producing adenoma of the left adrenal gland. A. The mass shows heterogeneous attenuation with patchy low attenuation area on non-enhanced CT. B. The mass presents moderately heterogeneous enhancement after contrast administration.

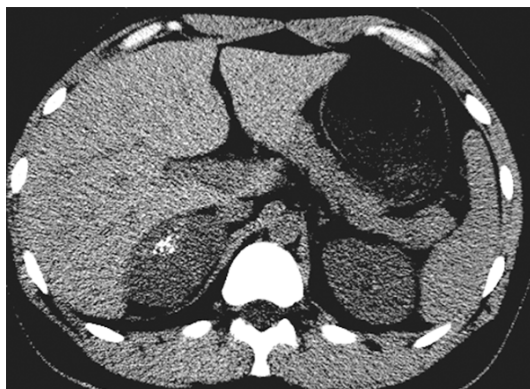


Figure 5. A 63-year-old male with non-functional adenoma of the right adrenal gland. The mass shows stippled calcification on non-enhanced CT.

each mass was compared with that of the muscles in the lateral abdominal wall.

Results

Clinical data

Large adrenal adenoma group: The clinical data of the 14 patients are summarized in **Table 1**. There was no sex and age predilection on the incidence of large adrenal adenoma. Eight patients who were proved as cortisol producing adenoma mainly complained of hypertension and headache. Six patients who were proved as non-functional adenoma felt uneventful, who, actually, were detected adrenal mass incidentally during abdominal CT scan for other reasons.

Adrenal carcinoma group: The clinical data of the 13 patients are summarized in **Table 2**. There was no sex and age predilection on the

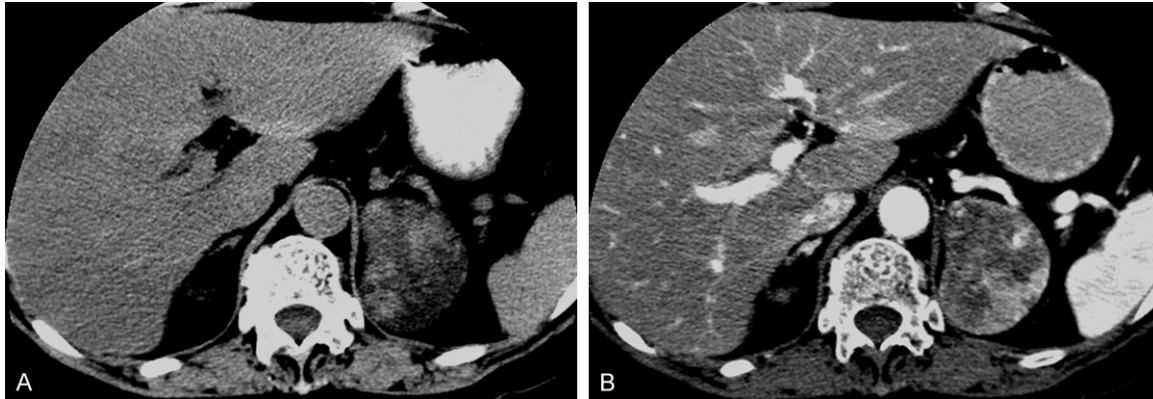


Figure 6. A 44-year-old male with non-functional adenoma of the left adrenal gland. A. The mass shows obviously heterogeneous attenuation on non-enhanced CT. B. The mass presents moderately heterogeneous enhancement after contrast administration.

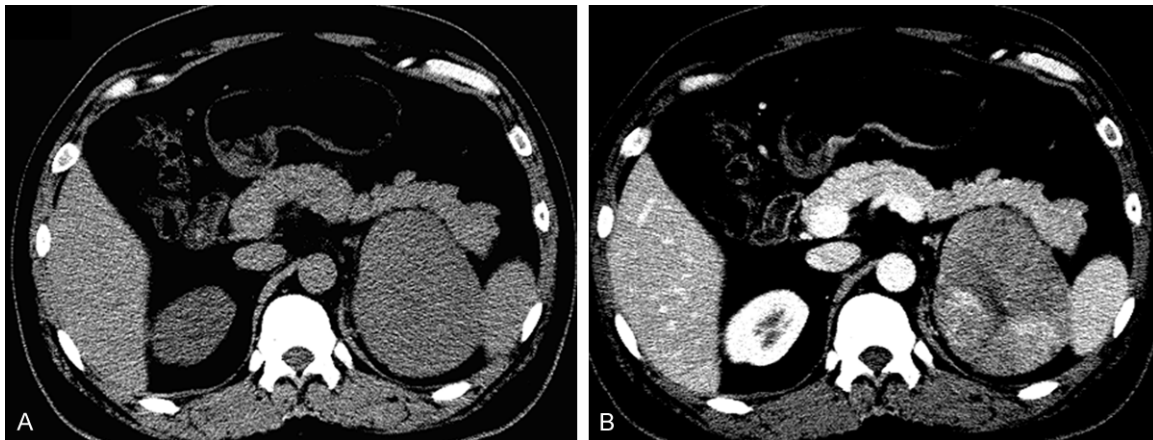


Figure 7. A 30-year-old male with cortical carcinoma of the left adrenal gland. A. The mass shows well-circumscribed, ovoid shape and homogeneous attenuation on non-enhanced CT. B. The mass presents moderately heterogeneous enhancement after contrast administration.

incidence of adrenal carcinoma. Of the 13 patients, 11 manifested endocrine dysfunction including Cushing syndrome, virilization, feminization, hyperaldosteronism, 2 old patients complained of abdominal pain and abdominal distention.

CT findings

Large adrenal adenoma group: All the 14 large adenomas were unilateral and single, a total of 14 masses, 6 of which were on the left and the other 8 masses were on the right. The maximal diameter of the 14 masses ranged from 5.5 cm to 20 cm (mean, 10 cm), of those, the maximal diameter of the cortisol producing adenoma and non-functional adenoma ranged from 5.5 cm to 10 cm (mean, 8 cm) and 8 cm to 20 cm

(mean, 12 cm), respectively. One mass showed lobulated (**Figure 1**), the rest 13 masses showed rounded or ovoid (**Figure 2**). Eleven masses appeared well-circumscribed (**Figure 2**) and 3 masses appeared ill-circumscribed (**Figure 3**). All the 14 masses presented heterogeneous density on non-enhanced CT images, 12 of which showed patchy low attenuation foci (**Figure 4**), 2 of which showed stippled calcification (**Figure 5**). After contrast administration, all the masses revealed moderately to markedly heterogeneous enhancement (**Figure 6**). None of the masses developed local invasion and distant metastasis.

Adrenal carcinoma group: All the 13 adrenal carcinomas were unilateral and single, a total of 13 masses, 7 of which were on the left and

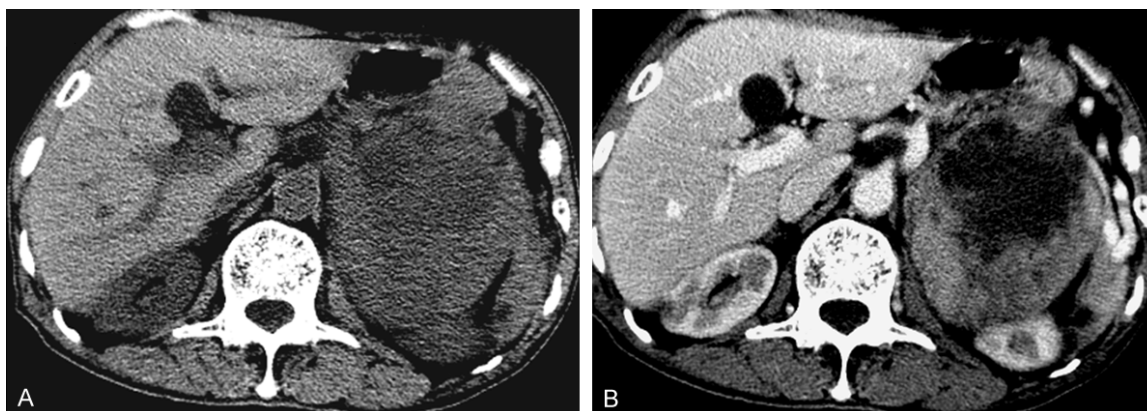


Figure 8. A 60-year-old male with cortical carcinoma of the left adrenal gland. A. The mass shows heterogeneous attenuation with patchy low attenuation area on non-enhanced CT. B. The mass presents moderately heterogeneous enhancement after contrast administration.



Figure 9. A 57-year-old female with a history of one year after the right adrenal cortical carcinoma resection. One mass recurs on the right surgical site presenting moderately heterogeneous enhancement after contrast administration, and the mass was confirmed pathologically as cortical carcinoma recurrence.

the other 6 masses were on the right. The maximal diameters of 13 masses ranged from 5.5 cm to 12 cm (mean, 8 cm). Three masses showed lobulated, the rest 10 masses showed rounded or ovoid (**Figure 7**). Seven masses appeared ill-circumscribed and 6 masses appeared well-circumscribed. All the 13 masses presented heterogeneous density on non-enhanced CT images, 12 of which showed patchy low attenuation foci (**Figure 8**), 3 of which showed stippled calcification. After contrast administration, all the masses revealed heterogeneous enhancement (**Figure 8**). Three, two and one patient developed recurrence after surgery (**Figure 9**), distant metastasis and

tumor thrombus into inferior vena cava (**Figure 10**), respectively.

Computed tomographic features that permitted confident differentiation between adenomas and carcinomas were found in 4 cases. Recurrence after surgery, metastases and tumor thrombus were present only in patients with carcinomas.

Discussion

Adrenal adenomas with the maximal diameter greater than 5 cm are benign entities originating from adrenal cortex and are considerably rare clinically. Because of gigantic mass and heterogeneous density on CT image, such tumors are more likely diagnosed as malignancies such as adrenal cortical carcinomas which usually confuse most surgeons due to the different treatment and prognosis for both tumors. Therefore, it is necessary to investigate the CT findings of large adrenal adenomas and determine whether differentiation of these lesions from adrenal carcinomas can be made by means of preoperative CT imaging.

With regard to the age of onset and sex of patients with large adrenal adenoma, there was no specificity in our study group, which was consistent with previous reports [1-7]. Clinically, most of 8 patients with cortisol producing adenoma complained of hypertension and headache, while all the 6 patients with non-functional adenoma didn't feel any unwell. Due to absence of symptoms, non-functional adenomas usually develop larger masses than do cor-

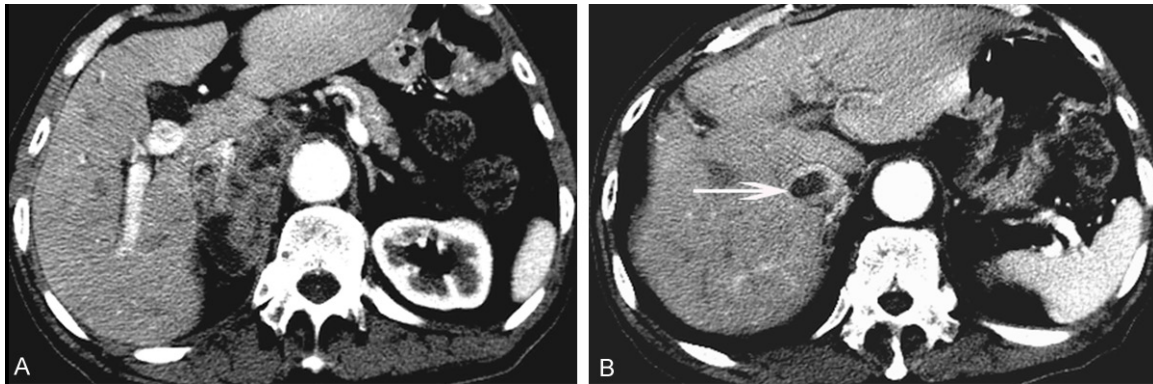


Figure 10. A 77-year-old male with cortical carcinoma of the right adrenal gland. A. The mass shows moderately heterogeneous enhancement after contrast administration. B. The patient presents tumor thrombus into inferior vena cava (arrowhead).

tisol producing adenomas when they are detected (mean maximal diameter of 12 cm of non-functional adenomas versus that of 8 cm of cortisol producing adenomas in our study group). On the other hand, this sign implies that large adrenal cortisol producing adenomas should be considered when the patients with adrenal masses complain of hypertension and headache without obvious motivation.

There were 14 large adrenal cortical adenomas in our study. Except one mass revealed lobulated, the rest 13 masses (93%, 13/14) revealed rounded or ovoid, and 11 masses (79%, 11/14) showed well-circumscribed, which suggested that the large adrenal adenoma grew relatively slowly and regularly and confirmed their non-invasive growth pattern. On the other hand, of the 13 cases of adrenal carcinoma, 10 (77%, 10/13) presented round or ovoid, and six (46%, 6/13) revealed well-circumscribed. Therefore, the shape and edge of mass are of no significant meaning for identification of both entities.

In our study series, all the 14 large adrenal adenomas presented heterogeneous attenuation on non-enhanced CT images, 12 (86%, 12/14) of which showed patchy low attenuation foci. After contrast administration, all the 14 masses showed moderately to markedly heterogeneous enhancement. According to reports in the literature [6, 8], the low-attenuation foci may represent cystic degeneration within the lesions. Newhouse JH et al [6] reported 30 patients with large adrenal adenoma, 17 of which appeared complete or partial cystic degeneration. Masugi Y et al [8] also reported

one patient with large adrenal adenoma which appeared extensive cystic degeneration. Also, other related documents [9, 10] reported that large adrenal adenoma was more likely to develop cystic degeneration. As for this point, our results are in accordance with literature report. We speculate that large adrenal tumors easily become ischemic and anoxic, and the ischemic and anoxic regions develop cystic degeneration eventually. However, in this study, 12 (92%, 12/13) masses of cortical carcinoma also manifested patchy low attenuation foci possibly representing necrotic lesions, which made the identification of large adenoma with cortical carcinoma quite difficult.

Only 2 (14%, 2/14) masses of large adenoma and 3 (23%, 3/13) masses of cortical carcinoma showed stippled calcification, respectively. Because of small sample size, we don't think the occurrence of calcification is helpful for the diagnosis of both large adrenal cortical adenoma and cortical carcinoma.

None of the large adrenal adenomas developed local invasion and distant metastasis on CT images, while three, two and one patient with cortical carcinoma developed recurrence after surgery, distant metastasis and tumor thrombus into inferior vena cava, respectively. These results indicated the benign and malignant biologic behaviour of large adenoma and cortical carcinoma, respectively, and, this finding was the only valuable identification between large adenoma and cortical carcinoma.

A potential limitation of the present study is the small sample size analyzed here, which may

lead to lack of certain CT findings of large adenoma. For example, according to some documentary literature [11-14], large adrenal lesion, no matter benign or malignant, may be prone to developing internal hemorrhage, while in this study cohort, no hemorrhage was detected in both large adenoma and cortical carcinoma. Therefore, we look forward to collecting more cases in the future so as to discuss this issue.

Conclusion

To sum up, the characteristic CT findings of adrenal cortical adenoma with the maximal diameter greater than 5 cm include bulky, well-circumscribed mass with rounded or ovoid shape, heterogeneous attenuation with low-attenuation foci on non-enhanced CT images and moderately to markedly heterogeneous enhancement after contrast administration. The tumor scarcely develops local invasion and distant metastasis. Such findings as recurrence, metastasis and venous tumor emboli are of some significance to the differential diagnosis between large adrenal adenoma and cortical carcinoma, while the exact identification of both lesions depends on pathological examination [15].

Disclosure of conflict of interest

None.

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